Review Article

A narrative review of type 2 diabetes mellitus and its management in children and adolescents

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Background and Objective: The rate of type 2 diabetes mellitus (T2DM) in children and adolescents has exponentially increased over the past two decades. Equally concerning is the increasing rate of childhood obesity. While the presence of childhood obesity does not infer development of T2DM, obesity does increase the inherent risk for developing obesity related co-morbidities including T2DM. This narrative aims to provide the reader with a comprehensive overview of current knowledge of T2DM in children and adolescents and its management, including update on new medications recently approved for use in this population.

Methods: We conducted a PubMed search including literature in the English language using keywords: type 2 diabetes, youth, children, adolescents, insulin resistance, diabetes education, obesity. We considered literature from reference of retrieved literature. We considered all literature published between January 2000 to July 2021.

Key Content and Findings: A comprehensive overview of current knowledge, management and treatment of T2DM in children and adolescents.

Conclusions: T2DM is characterized by persistent hyperglycemia in the setting of impaired glucose tolerance and relative insulin deficiency. Understanding the differences and similarities between type 1 diabetes mellitus (T1DM) and T2DM aids in proper diagnosis in youth who often have overlapping phenotypic presentation. Screening for T2DM in at risk youth is critical for timely diagnosis to ameliorate and reduce risk for development of co-morbidities that often present at time of diagnosis. Lifestyle modifications are the gold standard in the treatment and management of T2DM in children and adolescents. In recent years there has been widespread recognition that traditional management with oral medications and insulin fails to adequately treat youth with T2DM. Recent FDA approval of GLP-1 analogs for use in older children and adolescents provides clinicians additional management options, which have not only demonstrated improve glycemic control, but at higher doses, has shown clinically significant reduction in body mass index (BMI). Additionally, addressing obesity as a primary factor increasing risk and contributing to T2DM allows the provider, patient and family to consider metabolic bariatric surgery for symptom remission.

Keywords: Type 2 diabetes mellitus (T2DM); pediatrics; children; adolescents; obesity

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Introduction

Type 2 diabetes mellitus (T2DM) is a heterogeneous, complex metabolic disorder characterized by hyperglycemia, insulin resistance and impaired insulin secretion. Persistent hyperglycemia hastens pancreatic β-cell failure resulting in relative insulin deficiency (1). Unlike T1DM and T2DM in adults, T2DM in children and adolescence is associated with more rapid decline in β-cell function and accelerated development of diabetes related comorbidities (2). This narrative review highlights current understanding of disease development and clinical practice guidelines. We aim to provide discussion on current treatment and management that may be useful to the clinician caring for at risk children and adolescents. We present this article in accordance with the Narrative Review reporting checklist (available at https://pm.amegroups.com/article/view/10.21037/pm-21-103/rc).

Methods

A PubMed search was conducted considering literature published in English, published between January 2000 to July 2021, using the following keywords: type 2 diabetes, youth, children, adolescents, insulin resistance, diabetes education, obesity. Referenced literature from retrieved references was also considered (*Table 1*).

Epidemiology

Among children, T1DM remains the dominant form of diabetes over other types of diabetes, arguably posing the greatest risks (3). However, over the last two decades, the incidence and prevalence of T2DM have increased exponentially in children and adolescents, paralleling rates of childhood obesity. In 2009, over 20,000 US youth had T2DM (4). An estimated 3,700 youth are diagnosed with T2DM annually (5). Similarly, an estimated 39 million children under the age of 5 years are overweight or obese, and over 340 million youth aged 5–19 years are overweight or obese (6). Obesity is disproportionately higher in certain ethnic and minority race groups. Hispanic and non-Hispanic black youth are among those with the highest rates of obesity (7). Likewise, data from SEARCH for Diabetes in Youth Study report higher prevalence of T2DM in youth from similar ethnic and minority race groups: 5.5% for non-Hispanic white youth, while the proportion of T2DM among non-Hispanic blacks is 37.6%, American Indian/Alaskan Natives 80%, Asian/Pacific Islander 34.2% and Hispanic 35.2% (4). Perhaps more concerning is the projected fourfold increase in youth living with T2DM (4). If not properly addressed, T2DM among children and adolescents has the potential to become a global health crisis. It is critically important to acknowledge and understand the contribution of social determinants to the overall risks for developing T2DM and its management. Likewise, psychosocial factors also contribute similarly to the risk for developing and managing T2DM. Many youth who are at risk or have T2DM live in rural, underserved areas, live in poverty, or live in areas of food scarcity where equitable access to adequate health care and resources is lacking. While the importance of these inequities is important to address adequate treatment and management, the breadth and importance of this topic is too broad for this discussion and deserves its own discussion. The focus of this paper is an overview of T2DM and its management in regions with adequate resources and access to care.

Pathophysiology of T2DM

T2DM is characterized by insulin resistance in peripheral

Table 1 The search strategy summary

Items	Specification
Date of search	June 30, 2021
Database searched	PubMed
Search terms used	Type 2 diabetes, youth, children, adolescents, insulin resistance, diabetes education, obesity
Timeframe	January 1, 2000 to June 30, 2021
Inclusion and exclusion criteria	Articles not available in English were excluded. Otherwise, all retrieved literature was considered
Selection process	Each author independently searched and selected relevant literature

tissue (skeletal muscle, adipose and liver) exponentially increasing insulin demands to maintain normoglycemia. Inadequate insulin response, β-cell dysfunction, and relative β-cell failure in response to increased demands results in persistent hyperglycemia (8). Resultant persistence leads to the development of T2DM. It is widely known that genetics, physiological and environmental risk factors contribute to disease pathology. Early life exposures including maternal health, and alterations in metabolic and cellular function have been found to have profound effects contributing to greater risk for developing T2DM across the lifespan (9). Gestational diabetes, family history and ethnicity are additional risk factors predisposing youth to T2DM (4,5,9-11).

Genetic factors may be important to determine which youth are at greatest risk for developing obesity and T2DM. However, it does not fully explain why some youth develop obesity and why some youth with obesity develop T2DM and other youth with obesity do not develop T2DM. Perceived genetic risk may be associated with strong family prevalence. Rather than genetic risk as a factor contributing, it is likely shared lifestyles and socioeconomic risks that have the greatest impact determining why some groups of individuals are at greater risk for T2DM and then others (11,12).

Genome-wide association studies have identified several genes that affect insulin secretion and sensitivity (12,13). However, no gene has been identified that increases risk for development of T2DM. The *FTO* gene is the only gene, to date, that has been associated with predisposition for obesity in children as young as 7 years (12). The fat mass and obesity-associated (*FTO*) gene are multiple single nucleotide polymorphism sites associated with increased body mass index (BMI) and obesity in several different populations (14,15). *FTO* is expressed in human adipose tissue and skeletal muscle with highest expression in the region of the hypothalamus responsible for energy control (14) The exact mechanisms of FTO polymorphism and its high risk for obesity remains unclear.

Obesity is widely recognized as a major risk factor predisposing youth and adults to T2DM. Obesity, in the presence of a sedentary lifestyle and intake of excess calories, contributes to decreased insulin sensitivity. Persistent insulin resistance triggers a deleterious metabolic cascade increasing metabolites and signaling proteins (leptin, adiponectin and tumor necrosis factor-alpha) eventually leading to β-cell failure and insulin deficiency (11,16). Children with obesity have an approximate 40% reduction in insulin stimulated glucose metabolism as compared to their peers without obesity (11). Genetic syndromes such as Prader-Willi, Bardet-Biedl, Cohen syndrome, Trisomy 21, and Turner syndrome have associated increased risk for obesity and abnormal glucose metabolism leading to early onset of T2DM. Youth with Turner syndrome have an increased risk for impaired glucose tolerance independent of obesity (17).

Hormonal surges and fluctuations during puberty contribute to a unique variability of insulin sensitivity observed in pubertal adolescents regardless of BMI. Growth and sex hormones are implicated in exacerbating insulin resistance (18,19). Insulin sensitivity typically improves once puberty is complete. However, adolescents who are obese and have additional risk factors (i.e., poor diet, lack of physical activity, or family history) may have difficulty returning to euglycemia increasing their risk for T2DM in late adolescence and adulthood. Identifying post pubertal adolescents who are obese and who carry additional risk factors is important to target specific interventions to ameliorate risk.

Clinical presentation

Similar to T1DM, children and adolescents with T2DM may be symptomatic or asymptomatic at time of diagnosis. Symptoms may be present and disregarded for several years before diagnosis, increasing the child or adolescent's risk for obesity related comorbidities at time of diagnosis (20). Patients may present in diabetic ketoacidosis (DKA) due to the relative insulin deficiency or they may present with nonketotic hyperosmolar hyperglycemia state (HHS). Approximately 5% to 25% of patients newly diagnosed with T2DM present in DKA, while approximately 2% present in HHS (21). Classic symptoms of diabetes mellitus include hyperglycemia, polyphagia, polyuria, polydipsia, glucosuria, and ketonuria. History of weight loss may or not be present at time of diagnosis depending on the degree of insulin insufficiency. Patients may also present with concurrent infections such as skin fungal infections or vulvovaginitis due to Candida (1). Phenotypically, children and adolescents who are suspected to have T2DM are often overweight or obese.

With the rise in obesity, it is becoming increasingly more difficult to distinguish between phenotypical T1DM and T2DM in this population. Many T1DM patients are overweight or obese at the time of diagnosis. Adding to this difficulty is the presence of autoimmune antibodies in phenotypic T2DM youth at time of diagnosis. In the Treatment Options for Type 2 Diabetes in Adolescents

Table 2 Screening guidelines for children and adolescents at risk for developing type 2 diabetes

Child or adolescent who is overweight or obese (BMI >85th percentile, or >120% of ideal body weight)
Plus additional risk factors
• Maternal history of diabetes of gestational diabetes during pregnancy
• Family history of T2DM in first or second degree family member(s)
• Race/ethnicity (Native American, African American, Latino, Asian or Pacific Islander)
• Signs of insulin resistance (acanthosis nigricans)
• Comorbid conditions associated with IR/diabetes (hypertension, dyslipidemia, polycystic ovarian syndrome)
Screening labs
FPG, 2 h OGTT plasma glucose, or A1C

Screening recommended to begin after the age of 10 years or after onset of puberty, whichever comes first. Table adapted from reference (15). BMI, body mass index; T2DM, type 2 diabetes mellitus; IR, insulin resistance; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test.

and Youth (TODAY) study, 13.7% of youth with a clinical diagnosis of T2DM were positive for either GAD-65, IA2 antibodies, or both (22). Likewise, SEARCH for Diabetes in Youth study found 21.2% of children aged 10–19 years had + GAD-65 autoantibodies (23). While the significance of pancreatic autoantibodies in clinically diagnosed T2DM youth is unclear, adult studies in the UK have suggested more rapid failure of oral treatment in patients with autoantibodies than those without pancreatic autoimmunity (23). Individuals with autoimmunity appear clinically less like their autoantibody negative counterparts. Children and adolescents with autoimmunity are more likely to develop more rapid metabolic decomposition, requiring earlier exogenous insulin administration (21). Individuals with autoimmunity are less likely to be overweight or obese and have higher HDL level and lower triglyceride levels (23). C-peptide levels may be clinically useful in distinguishing those patients with T1DM versus T2DM. However, in the TODAY study, individuals with autoimmunity had lower C-peptide levels than the autoantibody negative group. Nonetheless, the presence of autoimmunity in overweight or obese children and adolescents can direct appropriate management and treatment to prevent significant morbidity (2,23).

Screening and diagnostic criteria for T2DM in youth

The increased prevalence of childhood obesity increases risk for development of T2DM in youth. Screening for T2DM is recommended for youth who are overweight (≥85th percentile) or obese (≥95th percentile), and who have additional risk factors as detailed in *Table 2*, including prediabetes (defined at HgbA1c of 5.7–6.4%) (24). Any one of the plasma glucose labs is appropriate for screening per the American Diabetes Association (ADA) recommendations for screening and diagnosis of diabetes. Diagnosis of diabetes is based on criteria defined by the ADA (*Table 3*). Additionally, because many youth may have co-existing comorbidities at time of diagnosis, blood pressure measurement, fasting lipid profile, random urine albumin-to-creatinine ratio and a dilated eye exam should be performed at the time of diagnosis (24,25).

Management

Youth with T2DM are at a higher risk of developing complications when compared to adults with T2DM or with other youth with T1DM (26,27). Recently published data from the TODAY study looking at long-term complications of youth onset T2DM showed that the risk of complications increased steadily over time and has affected most participants by the time of young adulthood (28). For this reason, a more aggressive and multidisciplinary approach to management, as soon as diagnosis, is necessary to prevent further complications and improve long-term outcomes.

Published guidelines from the American Academy of Pediatrics (AAP), International Society for Pediatrics and Adolescent Diabetes (ISPAD), and the American Diabetes Association (ADA) all recommend that a combination of lifestyle interventions and pharmacologic treatment is necessary (2,29,30). Involvement of several health professionals such as a pediatric endocrinologist, diabetes

Table 3 Diagnostic criteria for diabetes mellitus

A1C ≥6.5% (≥48 mmol/mol)
OR
FPG ≥126 mg/dL (7.0 mmol/mL)
OR
2 h plasma glucose ≥200 mg/dL (11.1 mmol/mL) during OGTT
OR
Classic symptoms of hyperglycemia (polyuria, polydipsia, polyphagia) or acute hyperglycemic crisis (DKA/HH) and random plasma glucose >200 mg/dL (11.1 mmol/mL)

Table adapted from reference (2) general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee (https://doi.org/10.2337/dc21SPPC). FPG, fasting plasma; OGTT, oral glucose tolerance test; DKA, diabetic ketoacidosis; HH, hyperosmolar hyperglycemia; ADA, American Diabetes Association.

educator, dietician, and mental health provider is essential, with a family-centered approach being most beneficial to ensure success of management.

Education

Education for diabetes self-management, directed not only for the patient but the whole family, is a crucial management goal (2,29). There is a stronger emphasis on lifestyle and behavioral intervention for individuals with T2DM. Depending on the glycemic control of the patient at diagnosis, the degree of pharmacologic intervention can vary, thus the daily routine of diabetes care may pose a greater challenge if requiring a more intensive regimen. The pediatric age group also pose the unique challenges of evolving physical, mental and psychologic development. In this regard, continued education and support from all team members should be a priority, ensuring that the approach should be tailored to age, culture and socio-economic status.

Non-pharmacologic management

Lifestyle interventions involve increasing physical activity, diet modification and behavior changes, with the goal of achieving BMI reduction through weight maintenance or weight loss. In a study of obese children without T2DM, a BMI decrease of >0.5 kg/m^2 was associated with improved insulin sensitivity, while in another study by Santoro, et al observed that a reduction of ~30% of excess weight may reverse impaired glucose tolerance in severely obese children and adolescents (29,30). The results of the TODAY study also demonstrated that sustained weight losses ≥7% of excess body weight were associated with improvements in A1C, HDL, and C-peptide levels (2).

Increased physical activity aids in weight reduction and improvement of insulin sensitivity, ultimately leading to better glycemic control (31,32). Participation in vigorous physical activity has also been associated with lower cardiovascular risks in youth with T2DM (33). Following recommendations of the AAP in the prevention and treatment of childhood overweight and obesity, youth are encouraged to participate in moderate to vigorous exercise for at least 60 min daily (33). Activities may comprise of several short segments throughout the day, with unstructured play being more appropriate for younger individuals and structured activities that youth enjoy, such as sports and dance, for older adolescents. Screen time should be limited to less than 2 h a day, aiming for reduced sedentary time. If available, consultation with an exercise or sports physiologist would be most beneficial, aiming for a more tailored approach depending on the individual's needs and capacity, while providing more structure and continued follow up.

Dietary recommendations provided by a dietician with experience in nutrition management for youth with diabetes should be appropriate culturally, and sensitive to the family's resources (34). Gradual dietary changes should focus on the following (35,36):

- Eliminating sugar-sweetened beverages;
- Increasing fruit and vegetable intake;
- Reducing consumption of processed and prepackaged foods;
- Reducing saturated and total fat intake;
- Increasing consumption of fiber-rich foods;
- Paying attention to portion control;

- ❖ Avoiding meals eaten away from home or while on screen time.

Participation of the whole family unit increases the chances of success and permanence of the dietary changes. Additional recommendations such as educating families on reading and interpreting nutrition labels, promoting scheduled meals as a family, and encouraging parents and caregivers to serve as role models to the children, are all encouraged (34).

Psychosocial factors are perhaps the biggest barrier to sustained lifestyle changes for individuals with chronic disease, including T2DM. Mental health issues are not uncommon in youth who are overweight or obese, while the burden of a chronic illness like diabetes adds to this. As many as 20% of youth with T2DM already have a psychiatric, neurodevelopmental or behavioral disorder at diagnosis (32). It is also established that youth-onset T2DM disproportionately affects youth from ethnic/minority groups, lower socioeconomic status, and have a family history of T2DM (37). As such, the comprehensive care of the youth with T2DM should include continued mental health support from an experienced provider that can guide the patient and family. Cognitive behavioral therapy and mindfulness interventions have been shown to improve depression, anxiety and glycemic control in adults (35). To date, there is still limited data on the effectiveness of these interventions in youth at risk for or already have T2DM.

Pharmacologic therapy

Initiation of pharmacologic therapy in conjunction with lifestyle changes has been the mainstay of treatment for youth onset T2DM. Initial therapy should aim for improvement of glycemia and addressing associated metabolic derangements, with adjustment of therapy once metabolic compensation has been achieved. As a significant percentage of youth-onset T2DM can present in ketoacidosis, management at diagnosis may not significantly differ that of T1DM. As such, the choice of pharmacotherapy would be influenced by degree of glycemic control and presence of acidosis at diagnosis, as well as results of pancreatic autoantibody testing to confirm or rule out T1DM. For patients with a hemoglobin A1c of <8.5% and are asymptomatic, metformin is the initial pharmacologic treatment of choice (2,29). Metformin is a biguanide that increases insulin-mediated glucose uptake in peripheral tissues and decreases hepatic glucose production (36). A gradual titration of dose starting at 500 to 1,000 mg daily, increased by increments of 500 to 1,000 mg ever 1–2 weeks to attain a maximal dose of 1,000 to 2,000 mg daily, helps reduce gastrointestinal side effects (29). Patients who experience gastrointestinal side effects may have better tolerance with extended-release metformin at the same dosing as regular metformin. In patients with marked hyperglycemia, HgbA1c of >8.5% but with no significant ketosis or ketoacidosis, metformin plus basal insulin therapy (0.25–0.5 U/kg/day as starting dose) is recommended for more rapid glycemic control. If glycemic targets are not attained on combination metformin and basal insulin therapy, intensification with the addition of rapid-actin insulin for meal coverage should be considered (2,29). Patients who present with ketoacidosis should be started on intravenous or subcutaneous insulin therapy immediately.

Biphasic insulin aspart (30/70) has been found to be a reasonable, and perhaps better alternative to both premixed insulin and basal-bolus regimens in terms of improved glycemic control.

Biphasic insulin aspart is composed of 30% rapid acting insulin and 70% intermediate acting insulin (basal). In a study of 372 T2DM patients who were insulin naïve, on metformin and sulfonylurea, ages ≥18 and ≤80 years old, researchers found significant improvement in glycemic control with use of biphasic insulin as part (38). Likewise, in a review of literature by Kumar, the author found improved glycemic control associated with the use of biphasic insulin aspart versus other insulins and oral diabetes medications (39). While these studies focused on the use of mixed insulin in adults, premixed insulin preparations are often used by prepubertal children in some countries (40). Despite the advantages of less frequent needle pokes and better glycemic control demonstrated in studies, the use of premixed insulin losses the flexibility and control of dosing the two separate insulins, particular in children with variable appetites, and use of mixed insulin has been found to have poorer glycemic control in adolescents (40).

Liraglutide, a GLP-1 receptor agonist that functions to slow gastric emptying, decrease appetite, enhance post-meal insulin production, suppress glucagon secretion and improve existing β-cell function to make more insulin, was approved by the FDA in June 2019 for the treatment of T2DM in pediatric patients >10 years of age. The approval came after the results of a clinical trial showing that liraglutide, when added to metformin, with or without basal insulin, was effective in improving glycemic control in children and adolescents with T2DM (41). More importantly, this was the first non-insulin drug approved for the treatment of T2DM in youth since metformin

was approved for pediatric use in 2010. This opened the door for subsequent non-insulin medications, currently used for adult T2DM, for consideration in the treatment of T2DM in youth. In July 2021, the FDA approved exenatide (Bydureon BCise), an extended release GLP-1 drug for use in youth >10 years for the treatment of T2DM. Exenatide offers a more appealing advantage over its former GLP-1 competitor, liraglutide, in that it is a once weekly injectable rather than a once daily injectable. While GLP-1 commonly cause gastrointestinal symptoms, such as nausea, vomiting and diarrhea, a once weekly injectable may encourage better treatment adherence in youth already at risk for poor adherence and compliance to their diabetes regimen. In a study of 83 youth, ages 10 years to less than 18 years, who were randomized into 2 groups (exenatide *vs.* placebo) for 24 weeks, youth treated with exenatide demonstrated a 0.36% reduction in glycated hemoglobin vs an increase of 0.49% in the placebo group. Additionally, youth treated with exenatide also demonstrated clinically significant improvement in fasting glucose levels, systolic blood pressure and body weight (42).

In addition to GLP-1 medications, there are a few recently completed and ongoing studies exploring the use of dipeptidyl peptidase-4 (DDP-4) and sodium-glucose co-transporter 2 (SGLT2) medications in the management of youth onset T2DM. Both classes of medications are currently used in adult T2DM management and may have the potential of not only providing additional options in the management of T2DM in youth but SGLT2 may also potentially provide improved cardiovascular and renal outcomes (43). In one study, the addition of sitagliptine, a DDP-4 inhibitor, to metformin did suggest durable glycemic control in youth with T2DM (44). More studies are needed to better understand why these medications provide glycemic control in adults but not in youth, taking into account factors such age of onset and rapidity of β-cell deterioration that may be contributing to differences observed.

Surgical therapy

Bariatric or metabolic surgery may be considered as treatment for youth with T2DM who have a BMI >35 kg/m^2, have other serious comorbidities, and failed to attain adequate glycemic control despite lifestyle and pharmacologic interventions (2,29). Several studies have shown the effectiveness of this intervention in adolescents (38,45-47). Surgical complications are infrequent, with most defined as minor (39). Micronutrient deficiencies, such as vitamin D, iron and folate, are common (40). As such, it is strongly recommended that this intervention should only be undertaken in centers of excellence with an established experience in pediatric surgical, nutritional, behavioral and medical support (27,28).

Complications

In our clinic, we encounter much of the inequities and psychosocial barriers mentioned in this article. Again, these barriers are deserving of their own discussion and the brief acknowledgement mentioned in this review does not begin to highlight the impact of these factors on short- and long-term outcomes. More recently, the COVID pandemic and increasing inflation only complicates family's ability to care and provide for themselves and their children, adding to an already difficult disease to manage. The recent approval of GLPs gives providers additional options in the treatment and management of T2DM in the pediatric population. However, it has been very difficult to prescribe these medications in our clinic due to lack of insurance coverage. While diet and physical activity remain the mainstay interventions, adherence to these recommendations are very low, equating to worsening disease and poor outcomes for our children and adolescents.

Youth with T2DM are at a higher risk of early diabetes related complications, including hypertension, dyslipidemia, albuminuria, and eye and nerve disease. In a recent prospective, longitudinal follow up study of the TODAY study cohort, the data revealed that complications appear early and progress rapidly in youth onset T2DM (28). Over 60% of the study participants developed one microvascular complication and 28.4% of participants had two or more complications at a mean age of 26.4 years. These findings not only highlight the concern for early onset diabetes complications but also emphasize the need for more aggressive management of T2DM in youth who are at risk for poor adherence and poor response to traditional management.

Summary

The etiology of T2DM is multifactorial. However, it appears that behavioral and environmental factors may play the greatest role. With the rising rates of diabetes paralleling the rates of obesity, screening for T2DM is recommended for all youth with risk factors associated

with obesity and insulin resistance. Youth who have an elevated A1C ≥6% but ≤6.5%, who are overweight or obese, and strong family history of T2DM are at greatest risk for developing T2DM and should be monitored closely. Children and adolescents often present with classic symptoms of diabetes. They may also present in DKA or HHS depending on the degree of insulin insufficiency. In the presence of overweight and obesity, correct diagnosis of the type of diabetes is not straightforward. Additional laboratory studies, such as c-peptide and autoantibodies, may provide insight and clarity on the type of diabetes. However, the presence of autoantibodies has been found in otherwise clinically diagnosed T2DM patients. The presence of autoimmunity has inferred a more rapid decline in metabolic tolerance, accelerating the need for exogenous insulin.

Lifestyle and behavioral modifications remain the gold standard to ameliorate the risk and management of T2DM. Increased physical activity and dietary changes should be promoted as effective approaches to reverse insulin resistance and stabilize weight. Family centered and patient centered education is a key management component. However, lifestyle modification alone or in combination with metformin continues to fail at providing adequate glycemic control in most youth. Less is known about the impact of psychosocial factors for youth with T2DM in comparison to youth with T1DM. SEARCH data identified an association between declining quality of life scores and A1C suggesting that pre-existing and worsening psychosocial health impacts overall treatment and management of T2DM (4).

Pharmacological management is necessary in youth who require a more aggressive approach to managing their diabetes. Metformin and/or basal insulin therapy may be used in patients with persistent hyperglycemia. In patients who are unable to attain glycemic control, the addition of rapid acting insulin for carbohydrate coverage is recommended. Immediate medical management with intravenous or subcutaneous insulin therapy is required for patients presenting in DKA.

GLP-1 receptor agonists, such as liraglutide and exenatide, have recently been approved for pediatric patients ≥10 years of age changing the landscape of T2DM management in an age group with high rates of metformin monotherapy failure. Long acting GLP-1, exenatide, offers the benefit of improved adherence given its once weekly administration. SGLT2 and DDP-4 have been effective in managing T2DM in adults but have not been found to have durable glycemic control in youth. Bariatric or metabolic surgery may also be considered as treatment for older children and adolescents. It is strongly recommended that patients be referred to an established center of excellence with experience in pediatric surgery that provides comprehensive nutritional, behavioral and medical support.

Continued research and public funding focusing on the prevention of pediatric obesity and T2DM should be high priority to address this global health concern. Long term complications associated with youth onset T2DM are occurring at an earlier age and with greater severity than adult onset T2DM. The high burden of these complications will substantially strain the resources of our health care system if we continue to be passive.

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